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| 09/546,201      | 04/10/2000  | John M. Polo         | 930049.464/1463.002 | 3605             |

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EXAMINER

FOLEY, SHANON A

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1648

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/546,201

### Applicant(s)

POLO ET AL.

### Examiner

Shanon Foley

### Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 26, 28-31 and 33-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 26, 28-31, 33-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

In the paper submitted November 28, 2003, applicant amended claim 26. Claims 26,28-31 and 33-44 are under consideration.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26, 28-31 and 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky, Jr. et al. (US 6,015,686), which is hereinafter referred to as "Dubensky", Cella et al. (Journal of Experimental Medicine. March 1, 1999; 189 (5): 821-829) and Chada et al. (US 5,736,388) for reasons of record.

Applicant argues that argues that Dubensky and Chada teach multiple vector constructs, rather than a single vector construct claimed.

Applicant's arguments as well as a review of the references have been considered, but are found unpersuasive. Claims 34-43 are drawn to a gene delivery vector comprising an expression cassette. Although the vector vehicle of Dubensky and Chada is layered by a two-stage mechanism that controls the expression of heterologous DNA, the vector of Dubensky and Chada is a singular expression construct.

Applicant further asserts that the references do not suggest an expression vector expressing double stranded RNA. Applicant argues that the references only teach expressing

multiple heterologous genes from the same construct, but not a non-gene (double-stranded RNA).

Applicant's arguments have been fully considered, but are found unpersuasive because Dubensky teaches expressing a non-gene, antisense RNA, that forms dsRNA and induces increased expression of gamma interferon, see column 23, lines 1-10. In addition, even if the interferon-inducing dsRNA formed from the antisense RNA of Dubensky is not equivalent to the interferon-inducing dsRNA instantly claimed, the non-gene antisense RNA of Dubensky is expressed by the same mechanism as the heterologous gene expressed. Further, claim 10 of Dubensky is drawn to expressing antisense RNA or a non-coding sequence (a non-gene) from the vector construct. These limitations encompass antisense RNA forming dsRNA. Therefore, Dubensky teaches expressing multiple heterologous inserts from a vector construct (see column 16, line 61 to column 17, line 29 as well as column 85, line 50 to column 94, line 18), whether or not these inserts express a gene or a non-gene.

Applicant also argues that Cella does not provide motivation for the skilled artisan to make a single construct encoding dsRNA and an antigen.

Applicant's arguments have been considered, but are found unpersuasive because the limitations discussed by applicant are provided in the teachings of Dubensky. Dubensky expressly teaches that an MHC class I and/or II response is induced in response to a viral antigen expressed by the construct, see column 37, line 35 to column 38, line 16. Dubensky also expressly teaches that the interferon-inducing dsRNA formed from antisense RNA boosts the expression of MHC class I antigens, see column 23, lines 5-10. Cella provides further motivation to express double-stranded RNA within the expression vector of Dubensky. Cella

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teaches that dsRNA induces interferon, protects against cytopathic effects of a virus in dendritic cells and increases the capacity of dendritic cells to prime T cells, see the abstract and the first two paragraphs in the discussion section on page 826. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to induce the production of interferon with double-stranded RNA to protect dendritic cells from viral infection and generate a CTL response to a viral infection, see page 821 and the first two paragraphs in the discussion section on page 826 of Cella et al., and elicit a specific immune response with the viral antigen of Dubensky.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for expressing a heterologous antigen and double-stranded RNA in the vector of Dubensky because Dubensky teaches that the expression vector is used to express multiple heterologous genes, see column 16, line 61 to column 17, line 29 and column 85, line 50 to column 94, line 18. Therefore, the instant construct would have been prima facie obvious in view of the teachings of Dubensky, absent unexpected results to the contrary.

Applicant discusses the difference between dsRNA and antisense RNA and argues that reference by the examiner to antisense RNA in column 23 in Dubensky is irrelevant to the instantly claimed constructs expressing dsRNA and not antisense RNA.

Applicant's arguments have been fully considered, but are found unpersuasive. As discussed above, Dubensky teaches expressing antisense RNA or a non-coding sequence (a non-gene) from the vector construct, see claim 10. As applicant points out at the bottom of page 20, antisense RNA forms stable complexes with mRNA. The complex referred to by applicant involves two strands of RNA, i.e., double-stranded RNA. Dubensky teaches that the antisense

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RNA expressed by the construct forms large quantities of dsRNA, see the previous citation of column 23. Therefore, the interferon-inducing double-stranded RNA formed from the antisense RNA of Dubensky is indistinguishable from the interferon-inducing double-stranded RNA instantly claimed.

Applicant further argues that since Dubensky and Chada do not teach or suggest a single expression cassette forming dsRNA and Cella is silent with regard to expression constructs, there is no motivation to arrive at the instant invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Dubensky teaches all of the recited elements of claim 26. The difference between the instant claims and the teachings of Dubensky is that Dubensky teaches different constructs expressing each element separately, see claims 1, 2, 9 and 10 for example, and the instant claims require the heterologous inserts to be expressed from the same construct by separate expression elements.

Dubensky and Cella et al. teach motivation to combine the heterologous sequences into one construct. Dubensky teaches that expression of heterologous antigens stimulate a specific immune response to the antigen, see column 37, line 35 to column 38, line 16 and double stranded RNA stimulates the production of interferon, see column 23, lines 5-8 of Dubensky.

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Cella et al. teach that induction of interferon by double-stranded RNA protects against cytopathic effects of a virus and increases the capacity of dendritic cells to prime T cells, see the abstract and the first two paragraphs in the discussion section on page 826. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to induce the production of interferon with double-stranded RNA to protect dendritic cells from viral infection and generate a CTL response to a viral infection, see page 821 and the first two paragraphs in the discussion section on page 826 of Cella et al. and elicit a specific immune response with the viral antigen of Dubensky.

The combination of Dubensky and Chada et al. provide further motivation to express the heterologous sequences of Dubensky within the same construct from different promoters to ensure adequate levels of expression of all heterologous genes, see column 26, lines 4-21 of Chada et al.

Therefore, more than one motivation for combining the expression of the heterologous sequences of Dubensky from different promoters within the same construct is specifically taught in the prior art.

A reasonable expectation of success in producing the claimed expression cassette is also found within the prior art. The eukaryotic layered vector initiation expression cassette of Dubensky is used to simultaneously express multiple heterologous genes, see column 16, line 61 to column 17, line 29 and column 85, line 50 to column 94, line 18. In addition, Chada et al. teach using different promoters to express different genes within the same multivalent construct to ensure adequate levels of expression of all genes, see column 26, lines 4-21. The teachings of Chada et al. are directly applicable to the construct of Dubensky because both references teach a

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eukaryotic layered vector initiation expression cassette, see claim 1 of Dubensky and column 14, lines 52-56 of Chada et al.

The prior art teaches all of the limitations instantly recited and provides more than one motivation for combining the expression of heterologous genes into a single expression cassette with a reasonable expectation of success. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

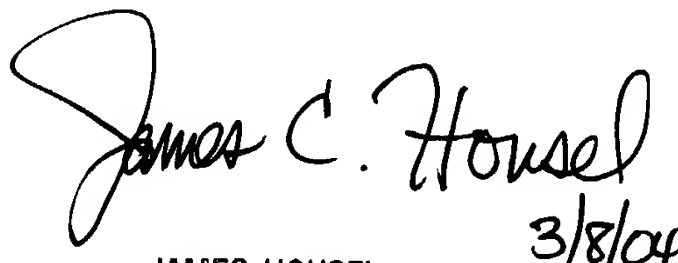


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Shanon Foley

  
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3/8/04